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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/596,194
Filing Date: June 02, 2006
Appellant(s): BARTHOLOMAUS, JOHANNES

HOWARD LEE
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 28, 2011 appealing from the Office action mailed April 29, 2011.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 6-25 and 18-22 are pending and rejected.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner.

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

US 6,780,504 B2	RUPPRECHT	08-2004
US 6,153,222	BECHER	11-2000
US 6,177,096 B1	ZERBE	01-2001
US 2003/0099692	LYDZINSKI ET AL.	05-2003

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites" the transmucosal or transdermal administration is buccal administration". However, as applicant has admitted in the specification, a buccal administration is limited to a transmucosal administration, as the buccal cavity is composed of mucosal membrane only. The presently limitation that a transdermal administration can be a buccal administration is inoperable and factually incorrect.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-15, 18-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rupprecht et al. (US 6780504 B2) ("Rupprecht") in view of Becher (US 6153222) and Zerbe et al. (US 6177096 B1) ("Zerbe").

Rupprecht discloses a dosage form in a multi-layered film which contains an active ingredient, wherein the dosage form comprises a cover layer, at least one active ingredient-containing layer and an adhesive layer. See col. 1, line 53 - 67; instant claims 1, 9, 10 and 18. Example 2 discloses such multi-layer film comprising 1 wt % prednisolone. See instant claim 22. The active ingredient-containing layer is formed from in-situ crosslinking of hydroxypropylmethylcellulose (MHPC) and tannin (a cross-linker) in water in presence of prednisolone. See Example 2, (b); see also Example 1; instant claims 1, 7. Rupprecht teaches to optimize the film properties by adjusting the ratio of polymer to crosslinking agent to from 1:1 to 4:1. See col. 3, lines 1-22; instant claim 21. The reference further teaches that the prior art multi-layer film dosage form allows the active ingredient to distribute uniformly over the whole layer, and that the active ingredient-containing layer exhibits horizontal and/or vertical gradients of the respective active ingredient. See col. 3, lines 51 – 67; instant claims 11 and 19.

The active ingredients suitable for application of the prior art dosage film form include nutrients, analgesics, antiallergic agents, antibiotics, antiemetics, antiseptics,

antihistamines, antihypertensive agents, appetite suppressants, cardiac remedies, chemotherapeutic agents, enzymes, hormones, immunomodulators, inoculations, local anesthetics, psychoactive drugs, spasmolytics, virustatics, vitamins, cytostatics, plant protection agent, growth promoter and/or fertilizer. See col. 4, lines 1-13; instant claims 7 and 8. Rupprecht teaches the prior art film is suitable in particular for use as a transmuosal medicament. See col. 8, lines 12 – 14; instant claims 1 and 15. Further including an additional barrier layer to the release side of the film to protect the release of the active agent is also taught. See col. 8, bridging par.; instant claims 13.

Rupprecht fails to teach adding glycerol in the active ingredient-containing layer of the film dosage form.

Becher teaches a dosage form in film of oral application, comprising a mixture of active ingredient, film former, and softeners. See abstract. The reference teaches using crosslinked carboxyvinyl copolymers and/or crosslinked polyvinyl pyrrolidone as film formers. See col. 2, lines 9-12. The reference teaches polyethylene glycol or glycerol as the softener. See Further substances. The film is supplied with release paper attached thereon, meeting instant claims 9, 13, and 18.

Becher fails to teach the amount of glycerol as based on the total amount of crosslinked hydrophilic polymers.

Zerbe teaches a film containing therapeutic agents and/or breath freshening agent for use in the oral cavity. See instant claims 5 and 6. The film comprises water-soluble polymers selected from water-soluble cellulose derivatives and polyacrylates, among others. The reference teaches the film also contains one or more plasticizers.

Example 1 teaches a dosage form in film form obtained from a composition comprising 6 g of glycerol and 30 g of hydroxypropylmethylcellulose (20% of glycerol based on the total amount of the hydrophilic polymer). See instant claims 1 and 3. The suitable pharmaceutical actives for the oral dosage forms include psychoactive drugs, antihistamines, hormones, antibiotics, and chemotherapeutics. See col. 3, lines 16 – 33.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Rupprecht by employing glycerol as a softener or plasticizer for the film as motivated by Becher and Zerbe. The skilled artisan would have been motivated to do so because 1) Becher teaches dosage forms in film forms that utilize glycerol as a plasticizer and 2) Zerbe discloses the weight amount of glycerol used per the weight amount of film-forming polymers used in similar formulations. Since Becher teaches adding glycerol with crosslinked film forming polymers, the skilled artisan would have had a reasonable expectation of successfully producing a stable film dosage form with improved and softened film properties.

Claim 1 requires the weight range of glycerol to from 30 % to 60 % by weight based on the total amount of crosslinked hydrophilic polymers. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA

1955). In this case, the utility of a plasticizer as a film softener is taught by Becher and Zerbe, and the latter teaches an operative weight amount of glycerol as plasticizer in a composition comprising a film forming polymer. Discovering by routine experimentations an optimal weight amount of the plasticizer for a different type of polymer such as the crosslinked hydrophilic polymer of Becher would take no more than ordinary skill of the art.

Claims 1, 6-15, 18-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rupprecht in view of Becher and Lydzinski et al. (US 2003/0099692).

Rupprecht and Becher are relied upon as discussed above.

Becher fails to teach the amount of the plasticizer.

Lydzinski teaches a dosage form in film form for delivering a variety of agents to a substrate, wherein the active agents may be pharmaceuticals such as dentifrice, antiseptics or agricultural agents such as fertilizers. See [0024]; instant claims 6-8. The reference teaches that plasticizers such as polyols, particularly glycerol, is used in "any desired amount" to increase the apparent flexibility of the film, although the prior art mentions using the plasticizer up to about 15 percent by weight of starch component which forms the bases for the prior art film form. See [0026].

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Rupprecht by employing glycerol as a softener or plasticizer for the film as motivated by Becher and Lydzinski. The skilled artisan would have been motivated to do so because 1) Becher teaches dosage forms

in film that utilize glycerol as a plasticizer and 2) Lydzinski discloses the specific weight amount of glycerol used per the weight amount of film-forming polymers used in similar formulations. Since Becher teaches adding glycerol with crosslinked film forming polymers, the skilled artisan would have had a reasonable expectation of successfully producing a stable film dosage form with improved and softened film properties.

With respect to the weight amount of the plasticizer, since Lydzinski teaches plasticizers are used in any desired amount and to increase flexibility of the film, the skilled artisan would have been obviously motivated to find an optimal weight amount of the plasticizer to obtain the desired level of flexibility. Doing so by routine experimentations would have been well within the skill of the art according to the teachings and suggestions of the references.

(10) Response to Argument

A. Claim 15 is vague and indefinite and properly rejected under 35 U.S.C. § 112, second paragraph.

Claim 15 depends on claim 1 and states, "the transmucosal or transdermal administration is buccal administration". Buccal administration is inherently transmucosal and cannot be transdermal. Appellant asserts that a person of ordinary skill in the art would understand that the scope of administration is limited to buccal administration. This statement is an admission that the claim is ambiguous, as a person of ordinary skill in the art would have to interpret the scope of the claim differently from how it is written.

B. Claims 1, 6-15 and 18-22 are properly rejected over Rupprecht in view of Becher and Zerbe under 35 U.S.C. § 103 (a).

Appellant asserts that a high amount of plasticizer leads to "phase separation" and crystallization of polymer films. Appellant base this argument on a single statement disclosed in the specification, which describes that addition of triethyl citrate at 30 wt % based on the total weight of a crosslinked hydrophilic polymer leads to white films. However, appellant has not established any correlation between triethyl citrate and glycerol, the plasticizer of instant claims; appellant has not provided any reasons why triethyl citrate and glycerol are expected to behave similarly.

As discussed in the rejection, in-situ crosslinked hydrophilic polymers has been used for dosage film in pharmaceutical art, and using glycerol as a film softener for dosage film was also well known. All oral dosage films exemplified in Zerbe specifically

teach glycerol and hydroxypropylmethylcellulose. It would have been prima facie obvious that a person of ordinary skill in the art would have used the same plasticizer, glycerol, to manipulate the plasticity of the in-situ crosslinked hydrophilic polymers of Rupprecht with a reasonable expectation of success.

Appellant asserts the facts of In re Aller are not analogous to the present application. See 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Appellant asserts that no inference is found in the references regarding result effect variable "within the context of their respective inventions". In response to this statement, examiner respectfully points out to col. 3, lines 10 – 16 which teaches using polyols to achieve the desired level of softness of the film", and discloses examples comprising glycerol and hydroxypropylmethylcellulose in different amounts. Thus manipulating the disclosed amounts of the plasticizer and polymer and increasing the amount of the plasticizer based on the polymer to produce more pliable film would have been well within the skill in the art.

Appellant's evidence of unexpected results

Appellant asserts Figures 1 and 3 in specification shows the use of glycerol in amounts greater than 20wt % resulted in more desirable products than when polyethylene glycol, sorbitol or triethyl citrate were used.

Figure 1 shows glycerol has a larger maximum elongation than films made from polyethylene glycol or sorbitol at concentration level of 25 %. Data is not commensurate with the scope of the present claims which require glycerol concentration of 30-60% based on the total amount of crosslinked hydrophilic polymers.

Furthermore, Zerbe teaches a specific example of utilizing glycerol, which already suggests glycerol is the most preferred plasticizer for oral dosage film products. Selection of glycerol would have been an obvious choice to one of ordinary skill in the art.

Figure 2 shows glycerol at 50 % wt based on the total amount of crosslinked hydroxypropylmethylcellulose produces a greater elongation and greater plasticity of the layers than at concentration of 20 %. However, it is viewed obvious that a greater amount of the film softener would produce greater plasticity or softness of the produced film. As discussed above, appellant's example of triethyl citrate and unidentified polymer in specification p. 2 does not bear any correlation to the present claims.

Figure 3 shows glycerol at 20 % wt shows a larger maximum elongation than triethyl citrate at the same concentration. Again, data here is not commensurate with the scope of the claims which require glycerol concentration of 30-60% based on the total amount of crosslinked hydrophilic polymers. Figure 3 actually indicates that glycerol and triethyl citrate behave differently at 20 %, thus differences between the two plasticizers at concentration of 30-60% is not surprising or unexpected.

C. Claims 1, 6-15 and 18-22 are properly rejected over Rupprecht in view of Lydzinski under 35 U.S.C. § 103 (a).

Appellant states that the present rejection is "essentially a duplicate rejection" and that "Lydzinski constitutes a weaker reference than Zerbe"; these assertions are erroneous and misleading. In fact, Lydzinski explicitly teaches polyols, particularly glycerol, is used in any desired amount to increase the apparent flexibility of the film. In

view of the prior art teaching here, a person of ordinary skill in the art would have reasonably expected that glycerol can be used at a high amount to increase the flexibility of polymeric film. Appellant's assertion that glycerol is somehow expected to behave as triethyl citrate does is unpersuasive and lacks support.

Examiner asserts the pending claims are prima facie obvious in view of the cited references as discussed above; appellant's arguments to overcome the rejections are unpersuasive and lack proper support or explanation.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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